

DECLARATION OF JOHN WIRONEN, Ph.D.
Examining Group 1615
Patent Application
Docket No. TB-101
Serial No. 08/816,079

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Alysia Berman
Art Unit : 1615
Applicants : Wironen *et al.*
Serial No. : 08/816,079
Docket No. : TB-101
Filed : 3/13/1997
For : Bone Paste

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF JOHN WIRONEN, Ph.D.

I John Wironen, Ph.D. hereby declare and say as follows:

THAT, I am employed as Senior Scientist at Regeneration Technologies Inc.;

THAT, I earned my Ph.D. in Materials Science and Engineering in 1997 from the University of Florida, Gainesville, Florida;

THAT, I am one of the above-named Applicants and inventors of the subject matter described and claimed in the above-identified patent application;

THAT, by virtue of my educational and employment background, my attendance at seminars, my continuing review of scientific periodicals and journals, and through correspondence with professional colleagues, I am aware of the level of skill of one ordinarily skilled in the art of bone substitutes, tissue engineering and materials engineering;

THAT, I have studied the application Serial No. 08/816,079 and all office actions which have been issued during prosecution of this application, as well as all responses which have been filed on the Applicant=s behalf, and being thus duly qualified declare as follows:

1. RTI currently sells a product under the name OSTEOPIL™, which pertains to a bone paste composition that comprises gelatin as a carrier for osteogenic components.

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OSTEOFIL™ has been on the market for nearly three years, and in this short period of time, OSTEOFIL™ has garnered sales of well over \$40 million. The rapidity and magnitude of the commercial success of this product is a remarkable occurrence in the orthopedics and bone repair market.

2. Further to the extraordinary commercial success the OSTEOFIL™ product has experienced, several recent studies highlight the fact that OSTEOFIL™ possesses unexpected, superior qualities over competitors' products, as recognized by those skilled in the art (see attached Exhibits A-D). The major products in this market, besides OSTEOFIL™, are GRAFTON™ gel or putty (Osteotech, Inc.) and DYNAGRAFT™ putty (GenSci, Inc.). Exhibits A-D represent comparative studies that evaluated the ability of these three products to induce generation of bone while monitoring for any deleterious side effects. In sum, these studies show that OSTEOFIL™ was the only product that demonstrated significant induction of bone without causing any harmful side effects. See Exhibit C, "An Unexpected Outcome During Testing of Commercially Available Demineralized Bone Graft Materials." With respect to DYNAGRAFT™, it simply failed to demonstrate bone induction when implanted into rats. See Exhibit A. On the other hand, GRAFTON™ showed a dose-dependent toxicity in rats and indeed, 8 of 9 rats died within 2 days when given doses of 0.0086 cc/g of GRAFTON™. These results compelled the authors to state that "[GRAFTON] must be used with extreme caution in lower weight pediatric patients and those at risk for renal disease. See Exhibit B.

3. The assertion in the office action mailed May 23, 2000 that claims 13, 14, 22, 23, 25, 26, and 33-37 are obvious over Scheicher in further view of O'Leary is incorrect. A reading of O'Leary clearly reveals that O'Leary does not teach the use of gelatin as a carrier agent. At column 3, lines 20-28, O'Leary defines the carrier as being a flowable liquid at 15-40 degrees Celsius when in a "pure or highly concentrated" form. Given my extensive experience in working with gelatin, it is my unequivocal opinion that gelatin would not be flowable at these temperatures in a pure or highly concentrated form. This and the fact that nowhere does O'Leary mention the use of gelatin as a carrier would

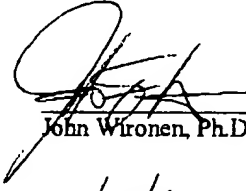
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cause those skilled in the art to conclude that gelatin is not intended as a carrier agent in the O'Leary composition.

4. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements in the like so made are punishable by fine or imprisonment, or both, under '1001 of' title 18 of the U.S.C. and that such willful false statements made jeopardize the validity of the application or of any patent issuing thereon.

Further declarant sayeth naught.



John Wironen, Ph.D.1/12/01

Date